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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,233	04/10/2001	John A. Kink	OPHD-06331	8942

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EXAMINER	
SHAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/832,233	KINK ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment filed on April 15, 2004 has been entered. Any rejection that is not addressed in this Office Action is considered Obviated in view of the Amendments and the Arguments.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1-5, 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Le et al US Patent 5,656,272, Eibl et al US Patent 5,833,984 ("Eibl II") in view of Wolf et al, (Acta Pediatr. supp. 1994, 396, 37-40), Muguruma et al (Prenat Neonat Med 1998;3:571-579), Eibl I (Acta Pediat 83,666-668, 1994) and Williams et al US Patent 5,601,823.

Le teaches anti-TNF antibodies for treating inflammatory bowel diseases such as Chrons disease (see abstracts, examples 1-3, claims 1-10). Le fails to specifically teach anti-TNF use for treating Neonatal Necrotizing Enterocolitis (NEC).

Eibl discloses methods of using anti TNF- antibodies to reduce the inflammatory response caused by gram-negative bacterimia (col 2, lines 7-10). Eibl further teaches the correlation between levels of TNF and the pathogenesis of neonatal NEC (see col 1, lines 60-66). Eibl further teaches various modes of administration of antibodies to a patient (col 6, lines 5-20). Eibl fails to specifically use anti-TNF antibodies in treating NEC.

The role of TNF in the development of neonate NEC has been well established in the art. Accordingly, Wolf, Eibl I and Muguruma are merely used to set forth general knowledge in the art about TNF and NEC.

Wolf, for example, describes the general knowledge about the affects of oral IgA-IgG preparations in inhibiting TNF release thereby preventing the development of pathological changes associated with NEC in low-birth-weight infants (p. 667, 4th para).

Eibl I sets forth successful use of IgA-IgG in treating or preventing NEC among human infants (see abstract, discussion).

Muguruma also teaches the role of TNF in the pathogenesis of NEC and ultimately the development of said condition specifically in low-birth-weight neonates (see abstract, entire document). Muguruma indicates the important role of pro-inflammatory agents such as TNF (page 575, 2nd, 3rd para-page 576, 2nd para.). Muguruma et al, however, fails to specifically teach the use of antibodies directed to PAF as a means of decreasing PAF activity among susceptible patients.

Eibl, Maguruma, and Wolf teach methods of treating conditions that are caused by over expression of pro-inflammatory factors, therefore, their teachings are viewed as being in the same field of endeavor.

Williams is merely used to show the state of art in formulating polyclonal avian antibodies for treating inflammatory enterocolitis caused by *Clostridium difficile*. (see abstract, col 21-col 24). Williams provides to one of ordinary skill in the art adequate teachings to prepare antibodies for treatment of gastric

inflammatory diseases similar to NEC. Neonates or infants can use the formulation of Williams. (see claim 3, col 1, line 44). Williams displays various advantages in using avian antibodies for oral administration. (col 9-11).

The role of TNF as a pro-inflammatory mediator in development of NEC has been well established in the art as shown by Maguruma, Wolf and Eibl I. Therefore, even though Le does not explicitly disclose the use of anti-TNF antibodies in treating NEC in neonates, it would have been obvious to one of ordinary skill in the art at the time of invention to employ such products for treatment of NEC, because as suggested by Eible II, Muguruma and Eibl I and Wolf, TNF plays an integral role in development of NEC and the ordinary skill in the art would have had a reasonable expectation of success in employing the anti-TNF of Le for treating NEC. Furthermore, one of ordinary skill in the art would have been motivated to formulate an avian polyclonal anti-TNF, because as suggested by Williams such type of antibodies can be administered orally, are non-immunogenic and are well tolerated by infants.

Additionally, it is well established that TNF potentiates the progress of NEC and thus reducing the effects of TNF activity among human infants would improve or alleviate the pathological changes that would lead to NEC. Examiner states that any degree of relief from NEC would read on the scope of the instant claims, and the ordinary skill in the art would have had a reasonable expectation of success in at least observing some symptomatic relief when administering the anti-TNF taught by Eibl.

Conclusion

No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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